

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of claims

1. – 41. (Canceled)

42. (Previously Amended) A process for production of plasmid DNA comprising:

(a) selecting a highly productive clonal subtype of a strain of *E. coli* transformed with a DNA plasmid comprising:

(i) observing a phenotypic heterogeneity in a population of colonies generated by the transformed *E. coli*, and selecting as potentially highly productive clonal subtypes those colonies that represent a minor component of said phenotypic heterogeneity in said population of colonies;

(ii) purifying said potentially highly productive clonal subtypes and determining the productivity of said purified, potentially highly productive clonal subtypes by measuring the plasmid copy number per cell; and,

(iii) selecting as a highly productive clonal subtype a potentially highly productive clonal subtype that exhibits a higher plasmid copy number per cell in comparison to non-selected, transformed *E. coli* clonal subtypes of the same strain; and,

(b) cultivating said highly productive clonal subtype with fed-batch fermentation in chemically-defined medium in a fermentation volume of greater than about 1000L, wherein said phenotypic heterogeneity is observed after the transformed *E. coli* is grown on blood agar at about 30°C, and

wherein the potentially highly productive clonal subtypes that represent the minor component of said phenotypic heterogeneity are gray colored-colonies while the major component of said phenotypic heterogeneity are white-colored colonies.

43. (Previously Presented) The process of claim 42, wherein the potentially highly productive clonal subtypes are purified from the blood agar.

44. (Previously Amended) The process of claim 43, wherein the plasmid copy number per cell of the purified, potentially highly productive clonal subtypes is determined after cultivating said clonal subtypes in a shake flask with feeding fermentation system using chemically defined medium.

45. (Previously Presented) The process of claim 44, wherein said strain of *E. coli* is DH5.

46. (Previously Presented) The process of claim 45, wherein said chemically-defined medium comprises a medium selected from the group consisting of Medium C, Medium D, Medium E, Medium F and Medium G.

47. (Currently Amended) The process of claim 42 44, wherein the process further comprises

(a) duplicate plating the transformed *E. coli* on blood agar and an agar that does not contain blood products;

(b) growing the *E. coli* at about 30°C until distinct colonies are visible;

(c) observing the gray colonies as the minor component of said phenotypic heterogeneity on the blood agar;

(d) determining which colonies on the agar that does not contain blood products correspond to of the gray colonies on the blood agar; and

(e) purifying said colonies from the agar that does not contain blood products that correspond to of the gray colonies on the blood agar,
wherein said purified colonies are the potentially highly productive clonal subtypes are purified by picking bacteria from colonies from a second type of agar that does not contain blood products, wherein said picked colonies correspond to the gray-colored colonies formed on the blood agar, and plating the bacteria picked from said colonies on said second type of agar.

48. (Previously Amended) The process of claim 47, wherein the plasmid copy number per cell of the purified, potentially highly productive clonal subtypes is determined after cultivating said clonal subtypes in a shake flask with feeding fermentation system using chemically defined medium.

49. (Previously Presented) The process of claim 48, wherein said strain of *E. coli* is DH5.

50. (Previously Presented) The process of claim 49, wherein said chemically-defined medium comprises a medium selected from the group consisting of Medium C, Medium D, Medium E, Medium F and Medium G.

51 - 55. (Canceled)

56. (Previously Presented) A process for production of plasmid DNA comprising:

- (a) selecting a highly productive clonal subtype of a strain of *E. coli* transformed with a DNA plasmid comprising:
- (i) observing a phenotypic heterogeneity in a population of colonies generated by the transformed *E. coli* when incubated on blood agar at 30°C consisting of a minor component of gray-colored colonies and a major component of white-colored colonies, and selecting as potentially highly productive clonal subtypes the gray-colored colonies;
- (ii) purifying said potentially highly productive clonal subtypes, and determining the productivity of said purified, potentially highly productive clonal subtypes by measuring the plasmid copy number per cell; and,
- (iii) selecting as a highly productive clonal subtype a potentially highly productive clonal subtype that exhibits a higher plasmid copy number per cell in comparison to non-selected, transformed *E. coli* clonal subtypes of the same strain; and,
- (b) cultivating said highly productive clonal subtype with fed-batch fermentation in chemically-defined medium.

57. (New) The process of claim 56, wherein said strain of *E. coli* is DH5.

58. (New) The process of claim 56, wherein said chemically-defined medium comprises a medium selected from the group consisting of Medium C, Medium D, Medium E, Medium F and Medium G.

59. (New) The process of claim 47, wherein the agar that does not contain blood products is a chemically-defined agar medium.